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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/716,842 | 11/17/2000 | Roger Briesewitz | STAN-131 | 8224 |

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| EXAMINER | |
|---|---|
| HUYNH, PHUONG N | |
| ART UNIT | PAPER NUMBER |
| 1644 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/716,842 | BRIESEWITZ ET AL. | |
| | Examiner | Art Unit | |
| | PHUONG HUYNH | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *6/30/08; 6/20/08*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *16-18, 22-26, 40-44, 46-50, 57-63 and 65-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-18,22-26,40-44,46-50,57-63 and 65-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

1. Claims 16-18, 22-26, 40-44, 46-50, 57-63 and 65-68 are pending.

2. The rejection of Claims 16-26 and 30-56 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 95/02684 publication (of record, published January 26, 1995; PTO 892) has been obviated by the claims amendments filed June 30 2008 and June 20, 2008.

3. The following new grounds of rejections are necessitated by the amendment filed June 30, 2008.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

5. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

6. Claims 16-18, 22-26, 40-44, 46-50, 57-63 and 65-68 are rejected under 35 U.S.C. 102(e) as being anticipated by US Pat No 6,372,712 B1 (claimed earliest priority to 60/084,451 filed May 22, 1998; PTO 892).

The '712 patent teaches a method for directing the biodistribution of a drug that binds to intracellular target by administering to a mammalian host such as a human (see col. 23, line 41-47, col. 25, lines 23-29, in particular) an effective amount of a bifunctional molecule having a molecular weight that does not exceed about 5000 daltons (see col. 17, lines 15-20, in particular) consisting of a drug moiety or an active derivative thereof (see col. 6, lines 39 through col. 13, line 67, and a targeting moiety (intracellular presenter protein) such as peptidyl-prolyisomerase

ligand such as FK506 and rapamycin that bind to intracellular FKBP, or cyclosporine A that binds to intracellular cyclophilin (see col. 15, line 21-49, col. 16, lines 12-14, col. 19, lines 23 through col. 20, in particular). The reference bifunctional molecule binds to endogenous (naturally occurring) peptidyl-prolyl isomerase presenter proteins present in the host, i.e., FKBP, or cyclopilin into which the bifunctional molecule is introduced, see col. 19, lines 11-13, in particular). The reference method inherently exhibits enhanced efficacy and reduced toxicity of the drug upon administration to the mammalian host because of the enhanced affinity, binding specificity and/or selectivity of the targeting moiety as compared to free drug control (see col. 21, lines 1-25, col. 22-23, in particular). The reference bifunctional molecule may comprise a linking group such as L (see col. 6, line 1-6, claim 9 of the '712 patent, in particular). The reference bifunctional molecule/peptidyl-prolyl isomerase complex does not bind to calcineurin (see col. 16, line 28-32, in particular). Upon administration to the host, the reference bifunctional molecule inherently binds to the naturally occurring intracellular peptidyl-proly isomerase to form a tripartite complex (see Summary of invention, in particular). Thus, the reference teachings anticipate the claimed invention.

7. Claims 16-18, 22-26, 40-44, 46-50, 57-63 and 65-68 are rejected under 35 U.S.C. 102(e) as being anticipated by US Pat No 6,921,531 B2 (claimed earliest priority to 60/084,451 filed May 22, 1998; PTO 892).

The '531 patent teaches a method for directing the biodistribution of a drug that binds to intracellular target (see claims 1 and 6 of the '531 patent) by administering to a mammalian host such as a human (see claims 1-3 of the ''531 patent , in particular) an effective amount of a bifunctional molecule having a molecular weight that does not exceed about 5000 daltons (see claim 1 of the '531 patent, col. 17, lines 1-8, in particular) consisting of a drug moiety or an active derivative thereof (see col. 6, lines 21 through col. 13, line 63-67, and a targeting moiety (intracellular presenter protein) such as peptidyl-prolyisomerase ligand such as FK506 and rapamycin that bind to intracellular FKBP, or cyclosporine A that binds to intracellular protein cyclophilin (see col. 15, line 8-42, col. 19, line 10-15, in particular). The reference bifunctional molecule binds to endogenous (naturally occurring) peptidyl-prolyl isomerase presenter proteins present in the host, i.e., FKBP, or cyclopilin into which the bifunctional molecule is introduced, see col. 19, lines 11-13, in particular). The reference method inherently exhibits enhanced efficacy and reduced toxicity of the drug upon administration to the mammalian host because of

the enhanced affinity, binding specificity and/or selectivity of the targeting moiety as compared to free drug control (see col. 21, lines 5-25, in particular). The reference bifunctional molecule may comprise a linking group such as L (see col. 6, line 1-6, claim 8 of the '531 patent, in particular). The reference bifunctional molecule/peptidyl-prolyl isomerase complex does not bind to calcineurin (see col. 16, line 17-23, in particular). Upon administration to the host, the reference bifunctional molecule inherently binds to the naturally occurring intracellular peptidyl-proly isomerase to form a tripartite complex (see claim 10 of the '531 patent, in particular). Thus, the reference teachings anticipate the claimed invention.

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 16-18, 22-26, 40-44, 46-50, 57-63 and 65-68 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 6-10, 12-19 of U.S. Patent No. 6,921,531 B2 (issued July 26, 2005; PTO 892). Although the conflicting claims are not identical, they are not patentably distinct from each other because the species of the instant

claimed method anticipates the genus method of administering a drug to a host such as human in need of said drug, the improvement comprising: administering to said host an effective amount of a bifunctional molecule of less than about 5000 daltons consisting of said drug or a fragment thereof linked to a ligand for a presenter protein endogenous to said host, wherein said drug binds to a drug target and said ligand binds to a presenter protein that is not said drug target in the issued patent.

The '531 patent teaches a method for directing the biodistribution of a drug that binds to intracellular target (see claims 1 and 6 of the '531 patent) by administering to a mammalian host such as a human (see claims 1-3 of the ''531 patent , in particular) an effective amount of a bifunctional molecule having a molecular weight that does not exceed about 5000 daltons (see claim 1 of the '531 patent, col. 17, lines 1-8, in particular) consisting of a drug moiety or an active derivative thereof (see col. 6, lines 21 through col. 13, line 63-67, and a targeting moiety (intracellular presenter protein) such as peptidyl-prolyisomerase ligand such as FK506 and rapamycin that bind to intracellular FKBP, or cyclosporine A that binds to intracellular protein cyclophilin (see col. 15, line 8-42, col. 19, line 10-15, in particular). The reference bifunctional molecule binds to endogenous (naturally occurring) peptidyl-prolyl isomerase presenter proteins present in the host, i.e., FKBP, or cyclopilin into which the bifunctional molecule is introduced, see col. 19, lines 11-13, in particular). The reference method inherently exhibits enhanced efficacy and reduced toxicity of the drug upon administration to the mammalian host because of the enhanced affinity, binding specificity and/or selectivity of the targeting moiety as compared to free drug control (see col. 21, lines 5-25, in particular). The reference bifunctional molecule may comprise a linking group such as L (see col. 6, line 1-6, claim 8 of the '531 patent, in particular). The reference bifunctional molecule/peptidyl-prolyl isomerase complex does not bind to calcineurin (see col. 16, line 17-23, in particular). Upon administration to the host, the reference bifunctional molecule inherently binds to the naturally occurring intracellular peptidyl-proly isomerase to form a tripartite complex (see claim 10 of the '531 patent, in particular). Thus, the reference teachings anticipate the claimed invention.

As such, issuance of a patent to instant application anticipates the claims of the issued patent. Conversely, the claims of the issued patent would include the claims of instant application.

10. No claim is allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh, Ph.D. whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Thursday from 9:00 a.m. to 6:30 p.m. and alternate Friday from 9: 00 a.m. to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen B O'Hara can be reached on (571) 272-0878. The IFW official Fax number is (571) 273-8300.

13. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Phuong Huynh/
Primary Examiner, Art Unit 1644
September 12, 2008